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The mean residual life (mrl) function (F(x)) gives the expected remaining life of a patient at age x, where the underlying failure distribution is F. Reliabilists and biometricians have found it useful to categorize failure distributions by monotonicity properties of the mrl. In particular F is said to be a decreasing mean residual life (dmrl) distribution if (F(0)) is finite and for all (F(0)) for (F(0)). If the preceding inequality is reversed, F is said to be an increasing mean residual life (imrl) distribution. Hollander and Proschan (1975) have derived tests of (1)  $H_0$ : F is exponential, versus  $H_1$ : F is dmrl, and (2)  $H_0$  versus  $H_1$ : F is imrl. Their tests are based on a (complete) random sample  $X_1, \dots, X_n$  from F. Often, however, data are incomplete due to withdrawals from the study and patients still surviving at the time the data are analyzed. In this paper, we generalize the Hollander-Proschan tests to accommodate randomly censored data. Asymptotically distribution-free tests of  $H_0$  versus  $H_1$  are provided. The efficiency loss, due to the presence of censoring, is also investigated.

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# TESTS FOR MONOTONE MEAN RESIDUAL LIFE USING RANDOMLY CENSORED DATA

by

Yuan Yan Chen, Myles Hollander and Naftali A. Langberg

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Tests for Monotone Mean Residual Life Using Randomly Censored Data

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# Summary

The mean residual life (mrl) function  $\mathbf{e}_{\mathbf{p}}(\mathbf{x})$  gives the expected remaining life of a patient at age  $\mathbf{x}$ , where the underlying Failure distribution is  $\mathbf{F}$ . Reliabilists and biametricians have found it useful to categorize failure distributions by monotonicity properties of the mrl. In particular  $\mathbf{F}$  is said to be a decreasing mean residual life (dmrl) distribution if  $\mathbf{e}_{\mathbf{p}}(0)$  is finite and for all  $0 \le \mathbf{s} \le \mathbf{t}$ ,  $\mathbf{e}_{\mathbf{p}}(\mathbf{s}) \ge \mathbf{e}_{\mathbf{p}}(\mathbf{t})$ . If the preceding inequality is reversed,  $\mathbf{F}$  is said to be an increasing mean residual life (imrl) distribution. Hollander and Proschan (1975) have derived tests of (1)  $\mathbf{H}_0$ :  $\mathbf{F}$  is exponential, versus  $\mathbf{H}_1$ :  $\mathbf{F}$  is dmrl, and (2)  $\mathbf{H}_0$  versus  $\mathbf{H}_1'$ :  $\mathbf{F}$  is imrl. Their tests are based on a (complete) random sample  $\mathbf{X}_1$ , ...,  $\mathbf{X}_n$  from  $\mathbf{F}$ . Often, however, data are incomplete due to withdrawals from the study and patients still surviving at the time the data are analysed. In this paper, we generalize the Hollander-Proschan tests to accommodate randomly consored data. Asymptotically distribution-free tests of  $\mathbf{H}_0$  versus  $\mathbf{H}_1$  and  $\mathbf{H}_0$  versus  $\mathbf{H}_1'$  are provided. The efficiency loss, due to the presence of censoring, is also investigated.

#### 1. Introduction

Let X be a random variable denoting the time to the occurrence of an end-point event. The distribution function (df)  $F(x) = P(X \le x)$  is called the failure distribution of X;  $R_F(x) = 1 - F(x)$  is the survival function. The mean residual life (mrl) function corresponding to F(x) is

$$\varepsilon_{\mathbf{p}}(\mathbf{x}) = \{ \left[ R_{\mathbf{p}}(\mathbf{u}) d\mathbf{u} \right] / R_{\mathbf{p}}(\mathbf{x}) . \tag{1}$$

Key Words: Hypothesis tests; Mean residual life; Kaplan-Meier estimator; Right-censored data.

The quantity  $\varepsilon_{\rm F}({\rm x})$  is the expected remaining life of the patient at age x, and thus could also be written as  $\varepsilon_{\rm F}({\rm x}) = {\rm E}({\rm X} - {\rm x}|{\rm X} > {\rm x})$ .

The mrl is a function of central importance in reliability, biometry, and other disciplines where survivorship studies arise. Some examples where knowledge concerning  $\epsilon_{\rm p}(x)$  is desired include the following.

- (i) An engineer is testing a component to study its failure distribution. Natural questions include: what is the expected remaining life of the component given that it has functioned properly for 10 days?; for 100 days?; and so forth.
- (ii) A biometrician is studying the survival data of patients receiving estrogen for treatment of prostate cancer. The biometrician, physicians, and patients are interested in the mean residual life at 12 months, at 18 months, at 24 months, etc.
- (iii) A sociological experiment is performed in which the variable under study is the time X until a victim is extricated from a 'mishap" by receiving help from a passerby. How long will a victim, on the average, have to wait if he has received no help in the first 10 minutes?, twenty minutes?, etc.

Obviously many other examples where study of the mrl arises can be cited, and the above examples can be rephrased in different contexts.

Estimation of the mrl has received considerable attention in the literature. Suppose a random sample  $X_1, \ldots, X_n$  is available from F. A natural nonparametric estimate of  $\epsilon_F(x)$  is

$$\tilde{\varepsilon}_{F}(x) = \left[\left\{ \int_{x}^{\infty} \tilde{K}_{F}(u) du \right\} / \tilde{K}_{F}(x) \right] \cdot I[x < X_{(n)}], \qquad (2)$$

where  $X_{(n)}$  = maximum  $[X_1, X_2, ..., X_n]$ ,  $I[x < X_{(n)}] = 1$  if  $x < X_{(n)}$  and 0 otherwise, and  $\widetilde{R}_F(x)$  is the empirical survival function of the X's. That is,  $\widetilde{R}_F(x) = n^{-1}$ . (number of X's in the sample > x).

Bryson and Siddiqui (1969) plot  $\tilde{\epsilon}_F$  for survival data of leukemia patients. Yang (1978) established strong consistency of  $\tilde{\epsilon}_F$  on a finite interval [0, T] and also showed that the associated mrl process  $n^{\frac{1}{4}}\{\tilde{\epsilon}_F(x) - \epsilon_F(x)\}$  converges weakly to a Guassian process. Hall and Wellner (1979) strengthen Yang's results; in particular they extend her weak convergence result to the positive real line. Hall and Wellner also derive nonparametric simultaneous confidence bands for  $\epsilon_F(x)$ . Chiang (1960) focused on estimating the discretized life-table version of the mrl function.

Testing for properties of the mrl has received less attention in the literature even though reliabilists have found it useful to categorize failure distributions according to monotonicity properties of the mrl.

A failure distribution F is said to be a decreasing mean residual life (dmr1) distribution if the mean,  $\epsilon_{\rm R}(0)$ , is finite and,

$$\varepsilon_{\mathbf{p}}(\mathbf{s}) \ge \varepsilon_{\mathbf{p}}(\mathbf{t}), \text{ for all } 0 \le \mathbf{s} \le \mathbf{t}.$$

F is said to be an *increasing mean residual life* (imrl) distribution if  $\epsilon_{\rm F}(0)$  is finite and the inequality in (3) is reversed.

The class of dmrl distributions is useful for modeling situations where lifelengths of items deteriorate with age, whereas the class of imrl distributions is appropriate for models where lifelengths improve with age. The boundary members of the dmrl and imrl classes, obtained by requiring equality in (3), are the exponential distributions. Of course, the exponential distributions can be used to model situations where lifelengths neither improve nor deteriorate with age. Equivalently, they are the distributions for which the mrl function  $e_p(x)$  is constant for all x.

Hollander and Proschan (1975) [HP(1975)] consider the problem of testing

$$H_0$$
:  $F(x) = 1 - \exp(-x/\mu)$ ,  $x \ge 0$ ,  $\mu > 0$ ,  $\mu$  unspecified, (4)

versus

H<sub>i</sub>: F is a durl distribution and is not exponential,

(5)

using a random sample  $X_1, \ldots, X_n$  from F. Significantly large values of their test statistic V\* lead to the rejection of  $H_0$  in favor of  $H_1$ . Significantly small values of V\* lead to the rejection of  $H_0$  in favor of

HP(1975) establish asymptotic normality of V\* and also provide critical values, obtained by Monte Carlo simulation, for n = 2(1)20(5)50. Exact critical values for n = 2(1)20(5)60 are given by Langenberg and Srinivasan (1979).

Bryson (1974) has suggested a test of  $H_0$  vs.  $H_1$ . However he gives critical values only for n = 10, 15, 20, 25, and 30, he does not derive the asymptotic distribution of his test statistic, and his test can not be easily converted to a test of  $H_0$  versus  $H_1$ .

In this paper we generalize the HP(1975) test to accommodate the randomly censored model. Thus, instead of a complete sample  $X_1, \ldots, X_n$ , we are only able to observe the pairs

$$Z_i = \min(X_i, T_i)$$
,  $\delta_i = 1$  if  $Z_i = X_i$  (ith observation is uncensored), and
$$= 0 \text{ if } Z_i = T_i \text{ (ith observation is censored)}.$$

We assume that  $X_1$ , ...,  $X_n$  are independent and identically distributed (i.i.d.) according to the continuous failure df F,  $T_1$ , ...,  $T_n$  are i.i.d. according to a continuous censoring df H(x) = P(T  $\leq$  x), and the T's and X's are mutually independent. The censoring df H is typically, though not necessarily, unknown and is treated as a maisance parameter.

Model (7) is useful because in many situations the data are analyzed before all the subjects have experienced the end-point event. For example, in situation (i) described earlier, some components on test will still be functioning when the test ends; in situation (ii) some patients will have dropped out of the study (by moving to another city, for example) and others will still be alive at data-analysis time; in situation (iii) some victims will still be awaiting extrication when the experiment ends.

In Section 2 we derive our test statistic, denoted by  $V^C$ . The derivation is similar to the approach of HP(1975), but whereas their derivation utilized the empirical df to estimate F, our statistic is formed by using the Kaplan-Meier estimator (1958) [KM(1958)] to estimate F.

Using results of Reid (1979), we show (in Appendix I) that  $V^C$ , suitably standardized, is asymptotically normal. The null asymptotic mean of  $V^C$  is 0, independent of the nuisance parameters  $\mu$  and H. However, the null asymptotic variance of  $n^2V^C$  (given by (A.4)) does depend on  $\mu$  and H and must be estimated from the data. A consistent estimator  $\hat{\tau}_0^2$  is also presented in Section 2. (The development of  $\hat{\tau}_0^2$  is given in Appendix I.)

In Section 3, by comparing the  $V^C$  statistic with the HP(1975)  $V^*$  statistic, we derive a measure of the efficiency loss incurred due to the presence of censoring.

In Section 4 we apply the  $V^C$  statistic to some prostate cancer survival data considered earlier by Koziol and Green (1976) and Hollander and Proschan (1979).

2. A Test for Monotone Nean Residual Life Using Randomly Ceneored Data Let  $D(s, t) = R_p(s)R_p(t)\{\varepsilon_p(s) - \varepsilon_p(t)\}$ . Then D(s, t) is, for s < t, a weighted measure of the deviation from  $H_0$  (exponentiality) to  $H_1$  (dmrl alternatives). The weights  $R_p(s)$  and  $R_p(t)$  represent the proportions of the population still alive at times s and s, respectively. Note that s of for all  $s \le t$  if and only if s is true. HP(1975) were thus led to consider

$$\Delta(F) = \int_{s < t} R_{F}(s) R_{F}(t) \{ \epsilon_{F}(s) - \epsilon_{F}(t) \} dF(s) dF(t)$$
(8)

as an average value of the deviation D. Straightforward calculations show that  $\Delta(F)$  can be rewritten as

$$\Delta(F) = \int_{0}^{\pi} (\frac{1}{2})F(u) - (\frac{3}{2})F^{2}(u) + (\frac{4}{3})F^{3}(u) - (\frac{1}{3})F^{4}(u)du.$$
 (8')

HP(1975) formed their statistic by replacing F by the empirical distribution function  $\tilde{F}$  in (8).

In our randomly censored model, the empirical distribution cannot be computed but we can compute  $\hat{F}$ , the KM(1958) estimator of F. Letting  $Z_{(0)} = 0$ , and  $Z_{(1)} < Z_{(2)} < \dots < Z_{(n)}$  denote the ordered Z's, and  $\delta_{(i)}$  the  $\delta$  corresponding to  $Z_{(i)}$ , we have

$$\hat{R}_{F}(x) = 1 - \hat{F}(x) = \prod_{\{i:Z_{(i)} \le x\}} [(n - i)(n - i + 1)^{-1}]^{\frac{6}{3}(i)}.$$
 (9)

In (9) we treat  $Z_{(n)}$  as an uncensored observation whether it is uncensored or not. Although ties have probability zero under our assumptions, in practice ties will occur. When censored observations are tied with uncensored observations, the convention when forming the list of ordered  $Z_{(i)}$ 's is to treat the uncensored members of the tie as preceding the censored members of the tie.

KM(1958) show that  $\hat{F}$  is the maximum likelihood estimator of F in the censored nonparametric model where no parametric assumptions about F are made. Asymptotic properties of  $\hat{F}$  are studied by Efron (1967), Breslow and Crowley (1974), Meier (1975), and Peterson (1977). Peterson also presents a summary of properties of  $\hat{F}$ .

To form our test statistic, we replace F by  $\hat{F}$  in (8'). Since  $\Delta(\hat{F})$  is not scale invariant, in order to make our test scale invariant we use the test statistic

$$\mathbf{V}^{\mathbf{C}} = \Delta(\hat{\mathbf{F}})/\hat{\mu},\tag{10}$$

where  $\hat{\mu}=\int\limits_0^R \hat{R}_F(x) dx$  is, under the assumption that the mean  $\int\limits_0^R R_F(x) dx$  is finite and under suitable regularity on the amount of censoring, a consistent estimator of  $\mu$ .

For computational purposes, use

$$\hat{\mu} = \sum_{i=1}^{n} [\pi[(n-j)/(n-j+1)]^{\delta(j)}](Z_{(i)} - Z_{(i-1)}).$$
 (11)

For computational purposes it is also helpful to rewrite  $\Delta(\hat{F})$  as

$$\Delta(\hat{F}) = \sum_{i=1}^{n} (-(1/6) \prod_{j=1}^{i-1} (n-j)/(n-j+1) \prod_{j=1}^{\delta(j)} + (\frac{1}{2}) \prod_{j=1}^{i-1} (n-j)/(n-j+1) \prod_{j=1}^{2\delta(j)} (12)$$

$$-(1/3) \prod_{j=1}^{i-1} (n-j)/(n-j+1) \prod_{j=1}^{4\delta(j)} \cdot (Z_{(i)} - Z_{(i-1)}).$$

A consistent estimator  $\hat{\tau}_0^2$  of the null asymptotic variance of  $n^{\frac{1}{2}\sqrt{C}}$  is developed in Appendix I. For computational purposes  $\hat{\tau}_0^2$  can be written as

$$\hat{\tau}_{0}^{2} = 726^{-1} + \sum_{i=1}^{n-1} n(n - i + 1)^{-1}(n - i)^{-1} \{72^{-1} \exp(-2\hat{\mu}^{-1} Z_{(i)})\}$$

$$- 18^{-1} \exp(-3\hat{\mu}^{-1} Z_{(i)}) + 16^{-1} \exp(-4\hat{\mu}^{-1} Z_{(i)})$$

$$+ 45^{-1} \exp(-5\hat{\mu}^{-1} Z_{(i)}) - 18^{-1} \exp(-6\hat{\mu}^{-1} Z_{(i)})$$

$$+ 72^{-1} \exp(-8\hat{\mu}^{-1} Z_{(i)})\} + n\{72^{-1} \exp(-2\hat{\mu}^{-1} Z_{(n)})$$

$$- 18^{-1} \exp(-3\hat{\mu}^{-1} Z_{(n)}) + 16^{-1} \exp(-4\hat{\mu}^{-1} Z_{(n)})$$

$$+ 45^{-1} \exp(-5\hat{\mu}^{-1} Z_{(n)}) - 18^{-1} \exp(-6\hat{\mu}^{-1} Z_{(n)})$$

$$+ 72^{-1} \exp(-8\hat{\mu}^{-1} Z_{(n)})\},$$

$$(13)$$

where  $\hat{\mu}$  is defined by (11).

To test  $H_0$  versus  $H_1$  at the approximate  $\alpha$ -level, reject  $H_0$  in favor of  $H_1$  if  $n^2 \nabla^2 \hat{\tau}_0^{-1} > z_\alpha$ , and accept  $H_0$  otherwise. Here  $z_\alpha$  is the upper  $\alpha$  percentile point of a standard normal distribution.

To test H<sub>0</sub> versus H<sub>1</sub>' at the approximate  $\alpha$ -level, reject H<sub>0</sub> in favor of H<sub>1</sub>' if  $\eta^2 V^C \hat{\tau}_0^{-1} < -z_\alpha$ , and accept H<sub>0</sub> otherwise.

Insisting that the null asymptotic variance of  $n^{\frac{1}{2}}V^{C}$ , as given by (A.4) of Ampendix I, be finite imposes a restriction on the amount of censoring that can be tolerated by the test based on  $V^{C}$ . The right-hand-side of (A.4) fails to converge if  $R_{K}(x) = 0\{R_{F}^{2}(x)\}$  as x approaches  $\infty$ . Consider this condition in the proportional hazards model where  $R_{H}(x) = \{R_{F}(x)\}^{Y}$ . Here  $\gamma$  is viewed as a censoring parameter since the probability that an observation will be censored is  $P(\delta_{1} = 0) = \gamma/(\gamma + 1)$ . Then, in this model, the right-hand-side of (A.4) is finite if  $\gamma < 1$ . Thus, for the proportional hazards situation, the  $V^{C}$  test will be inappropriate when the expected proportion of censored observations is greater than or equal to  $\frac{1}{2}$ .

# 3. Efficiency Loss Due to Censoring

Since the  $V^C$  statistic introduced in this paper is a generalization of the HP(1975) V\* statistic, we find it natural to compare the power of the V\* test based on n observations in the non-censored case with the power of the  $V^C$  test based on n\* observations in the randomly censored model.

Thus, let  $F_{\theta}$  be a parametric family within the dmrl class with  $F_{\theta_0}$  being exponential. Then we assume the randomly censored model with  $F = F_{\theta}$  and with censoring distribution H. For a sequence of alternatives  $\theta_n = \theta_0 + cn^{-\frac{1}{2}}$  (with c > 0) tending to the null hypothesis, let  $\beta_n(\theta_n)$  be the power of the approximate  $\alpha$ -level  $V^{\alpha}$  test based on n observations in the uncensored model, and let  $\beta_n(\theta_n)$  denote the power of the approximate  $\alpha$ -level  $V^{\alpha}$  test based on n' observations in the randomly censored model. Consider n' = h(n) such that  $\lim_{n \to \infty} \beta_n(\theta_n) = \lim_{n \to \infty} \beta_n(\theta_n)$ , where the limiting value is between 0 and 1, and let  $k = \lim_{n \to \infty} n/n'$ . The value of k can be viewed as a measure of the efficiency loss due to censoring. The value of k is adapted from Pitman's (cf. Noether, 1955) measure of asymptotic relative efficiency but the interpretation of k must be modified because the tests based on  $V^{\alpha}$  and  $V^{\alpha}$  are not competing tests in the randomly censored model ( $V^{\alpha}$  cannot be applied to the data arising in the randomly censored model). Roughly speaking, for large n and dmrl alternatives close to the null hypothesis of exponentiality, the  $V^{\alpha}$  test

requires n/k observations from the randomly censored model to do as well as the V\* test applied to n observations from the uncensored model. Since  $V^C$  and V\* have the same asymptotic means, it can be shown that k reduces to the limiting ratio of the null asymptotic variance of  $n^{\frac{1}{2}}V^{\frac{1}{2}}$  to that of  $n^{\frac{1}{2}}V^{\frac{1}{2}}$ , namely,

$$k \stackrel{\text{def.}}{=} e_{H}(V^{2}, V^{*}) = (210^{-1})/\tau_{0}^{2},$$
 (14)

where  $\tau_0^2$  is given by (A.4). Note that k depends only on the censoring distribution H, and not on the parametric family  $F_\theta$  of dmrl alternatives. Hence we use the notation  $e_H(V^C, V^*)$ , rather than  $e_{F,H}(V^C, V^*)$ , in (14).

We consider the cases (i) where the censoring distribution is exponential,  $R_{H_1}(x) = 1$  for x < 0,  $R_{H_1}(x) = \exp(-\lambda x)$ , x > 0, and (ii) where the censoring distribution is piecewise exponential,  $R_{H_2}(x) = 1$  for x < 0, and for  $r = 1, \ldots, m$ ,  $R_{H_2}(x) = c_r \exp(-\lambda_r x)$ ,  $s_{r-1} < x \le s_r$ , and  $R_{H_2}(x) = c_m \exp(-\lambda_m x)$  for  $s_m < x$ , where  $c_r = \exp(-\sum_{i=1}^{r-1} \lambda_i (s_i - s_{i-1}) + \lambda_r s_{r-1})$  and  $s_0 = 0$ .

In order that  $\tau_0^2$ , given by (A.4), be finite, in case (i) we must impose the restriction  $\lambda < 1$ . Then from (A.4) (with  $\mu = 1$ ) and (14) we find

$$\mathbf{e}_{\text{H}_{1}}(V^{c}, V^{*}) = (6/35)\{(1 - \lambda)^{-1} - 6(2 - \lambda)^{-1} + 9(3 - \lambda)^{-1} + 4(4 - \lambda)^{-1} - 12(5 - \lambda)^{-1} + 4(7 - \lambda)^{-1}\}^{-1}.$$
(15)

Values of  $e_{H_1}(V^C, V^*)$  are given in Table 1. Note, from (15), that as  $\lambda$  tends to 0 (corresponding to the case of no censoring), as expected we have  $e_{H_1}(V^C, V^*)$  tends to 1.

In order to provide a reference point to the amount of censoring, and thereby facilitate the interpretation of  $e_{H_1}(V^C, V^*)$ , we also include in Table 1 the value of  $p_{H_1} = P(X < T) = (1 + \lambda)^{-1}$ , the probability of obtaining an uncensored observation when X is exponential with scale parameter 1 and T is independent of X and has the censoring distribution  $H_1$ .

When the censoring distribution is  $H_2$ , again in order that  $\tau_0^2$  be finite we must impose the restriction  $\lambda_m < 1$ . Straightforward but tedious calculations yield

$$\begin{aligned} \mathbf{e}_{\text{H}_{2}}(\mathbf{V}^{\text{C}}, \, \, \mathbf{V}^{\text{A}}) &= (6/35) \{ \sum_{r=1}^{m+1} \mathbf{c}_{r}^{-1} [ \, (1 - \lambda_{r})^{-1} \{ \exp[-(1 - \lambda_{r}) \mathbf{s}_{r-1}] - \exp[-(1 - \lambda_{r}) \mathbf{s}_{r}] \} \\ &- 6(2 - \lambda_{r})^{-1} \{ \exp[-(2 - \lambda_{r}) \mathbf{s}_{r-1}] - \exp[-(2 - \lambda_{r}) \mathbf{s}_{r}] \} + 9(3 - \lambda_{r})^{-1} \{ \exp[-(3 - \lambda_{r}) \mathbf{s}_{r-1}] \\ &- \exp[-(3 - \lambda_{r}) \mathbf{s}_{r}] \} \end{aligned}$$

+ 
$$4(4 - \lambda_r)^{-1} \{ \exp[-(4 - \lambda_r)s_{r-1}] - \exp[-(4 - \lambda_r)s_r] \} - 12(5 - \lambda_r)^{-1} \{ \exp[-(5 - \lambda_r)s_{r-1}] - \exp[-(5 - \lambda_r)s_r] \} + 4(7 - \lambda_r)^{-1} \{ \exp[-(7 - \lambda_r)s_{r-1}] - \exp[-(7 - \lambda_r)s_r] \} ]^{-1},$$
where  $s_{m+1} = \infty$ .

Values of  $e_{H_2}(V^c, V^*)$  are also given in Table 1. Again, as a reference point for the amount of censoring under  $H_2$ , we include in Table 1 values of  $p_{H_2} = P(X < T)$  when X is exponential with scale parameter 1, and T is independent of X with distribution  $H_2$ . Direct calculations show

$$p_{H_{2}} = 1 - \sum_{r=1}^{m+1} c_{r} \lambda_{r} (1 + \lambda_{r})^{-1} [\exp\{-(\lambda_{r} + 1)s_{r-1}\} - \exp\{-(\lambda_{r} + 1)s_{r}\}],$$
where  $s_{m+1} = \infty$ .

#### [Insert Table 1 here.]

### 4. Example

The data in Table 2 were analyzed in Hollander and Proschan (1979) [HP(1979)] and are an updated version of data considered by Koziol and Green (1976). The data correspond to 211 state IV prostate cancer patients treated with estrogen in a Veterans Administration Cooperative Urological Research Group (1967) study. At the March, 1977

closing date there were 90 patients who died of prostate cancer, 105 who died of other diseases, and 16 still alive. The latter 121 observations are treated as censored observations (withdrawals).

Figure 1 of HP(1979) gives a plot of the KM survival function  $\hat{R}_F$  for the data of Table 2. HP(1979) also applied several goodness-of-fit tests, including ones proposed by Koziol and Green (1976), Hyde (1977) and a test developed in HP(1979), to test the null hypothesis that F is exponential with mean 100 months. (As stated by Koziol and Green (1976), prior experience suggested that had the patients not been treated with estrogen, their survival distribution for deaths from cancer of the prostate could be taken to be exponential with mean 100.)

Although the tests applied in HP(1979) tended to support the postulated exponential distribution with mean 100, the two-sided P value for the Koziol-Green test was .14 suggesting that perhaps a different model could be more appropriate. Furthermore, Gregory (1979) analyzes the Table 2 data by new goodness-of-fit tests (which will, for some alternatives, be more powerful than those proposed by Koziol and Green (1976), Hyde (1977), and HP(1979)) and his tests do not support the postulated exponential distribution with mean 100.

Figure 1 of this paper plots the Kaplan-Meier analogue  $\hat{r}_F(\cdot)$  of the empirical mrl function (defined by replacing  $\hat{R}_F$  by  $\hat{R}_F$  in (2)) for the data of Table 2. Specifically

$$e_F(x) = \left[\left(\int_{x}^{\infty} \hat{R}_F(u)du\right)/\hat{R}_F(x)\right] \cdot I[x < Z_{(n)}].$$

Note that  $e_F$ , for the data of Table 2, tends to decrease up to around 25 months, then tends to increase up to about 70 months, and then decreases again.

Figure 1 suggests 'wearout", but does not strongly suggest a strictly decreasing mean residual life.

Application of the  $V^C$  test tends to confirm the "eye-ball" impression one gets from Figure 1. We obtain, from (10) - (12),  $V^C$  = .027, and from (13),  $\hat{\tau}_0^2$  = .066. We then find

 $(211)^{\frac{1}{2}}V^{C}\hat{\tau}_{0}^{-1} = 1.52$  with a corresponding one-sided P value of .064. Thus, with this objective analysis, we find that the test suggests "wearout" in the dmrl direction, but the test does not strongly suggest a strictly decreasing mean residual life.

[Insert Table 2 here.]

[Insert Figure 1 here.]

# Acknowledgments

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# Appendix I

A Consistent Estimator of the Null Asymptotic Variance of  $V^C$ 

Using straightforward algebra and integration we can write

$$V^{c} - \{\Delta(F)\mu^{-1}\} = (\hat{\mu})^{-1} \int xJ(\hat{F}(x))d\hat{F}(x),$$
 (A.1)

where

$$J(u) = -(1/2) - \Delta(F)\mu^{-1} + 3u^{2} + (4/3)u^{3}.$$

The term  $\int x J(\hat{F}(x)) d\hat{F}(x)$  is a Kaplan-Meier "L-statistic" and results of Reid (1979) can be used to show

$$n^{\frac{1}{2}} \int xJ(\hat{F}(x))d\hat{F}(x) \rightarrow N(0,\sigma^2)$$
 (A.2)

where

$$\sigma^{2} = \iint R_{F}(x) R_{F}(y) J(F(x)) J(F(y)) \int_{0}^{XAY} (R_{K}(u) R_{F}(u))^{-1} dF(u) dxdy, \qquad (A.3)$$

where  $R_K(u) = R_P(u)R_H(u)$  and  $x \wedge y = min(x,y)$ . Thus from (A.1) - (A.3) and Slutsky's theorem (cf. Cramer, 1946, pp. 254-255), we have

$$n^{\frac{1}{2}}[V^{C} - \{\Delta(F)\mu^{-1}\}] \rightarrow N(0,\mu^{-2}\sigma^{2}).$$

Under  $H_0$ , it can be shown that  $\mu^{-2}\sigma^2$  reduces to the right-hand-side of (A.4), namely

$$\tau_0^2 \stackrel{\text{def.}}{=} \int_0^1 g(z) \{R_k(-\mu \ln(z))\}^{-1} dz,$$
 (A.4)

8.0

where

$$g(z) = 36^{-1}(z - 6z^2 + 9z^3 + 4z^4 - 12z^5 + 4z^7).$$

When there is no censoring, i.e.  $R_H(x) \equiv 1$ ,  $0 < x < \infty$ , the right-hand-side of (A.4) reduces to 1/210, agreeing with the result for the asymptotic variance of  $n^2V^*$ , the HP(1975) statistic designed for the uncensored case.

A consistent estimator  $\hat{\tau}_0^2$  of  $\tau_0^2$  is obtained by replacing  $R_{K}$ , in (A.4), by  $\hat{R}_{K}$ , the empirical survival function of the Z's;  $\hat{R}_{K}(x) = n^{-1}$ . (number of Z's > x). The resulting estimator is given by the right-hand-side of (13).

TABLE 1 Efficiency Losses Under Exponential  $(H_1)$  and Piecewise Exponential  $(H_2)$  Censoring

		н <sub>2</sub>					
	λ:	1/2	1/3	1/4	1/10		
	e <sub>H1</sub> (V <sup>C</sup> ,V*):	.248	.435	.552	.805		
	PH1:	.667	.750	.800	.909		
		H <sub>2</sub>					
m = 1	<b>s</b> <sub>1</sub> :	1	1	1	2		
	(λ <sub>1</sub> ,λ <sub>2</sub> ):	(1/2,1/3)	(1/3,1/2)	(1/3,1/4)	(1/2,1/3)		
	e <sub>H2</sub> (V <sup>c</sup> ,V*):	.374	.290	. 513	.326		
	PH2:	.685	.728	.763	.671		
m = 2	(s <sub>1</sub> ,s <sub>2</sub> ):	(1/2,1)	(1/2,1)	(1/2,1)			
	$(\lambda_1,\lambda_2,\lambda_3)$ :	(1/2,1/3,1/4)	(1/4,1/3,1/2)	(1/2,1/5,1/10)			
	e <sub>H2</sub> (V <sup>c</sup> ,V*):	.475	.302	.645	·		
	p <sub>H2</sub> :	.718	.750	.765			

#### TABLE 2

# Survival Times and Withdrawal Times in Months for 211 Patients (with number of ties given in parentheses)

Survival times: 0(3), 2, 3, 4, 6, 7(2), 8, 9(2), 11(3), 12(3), 15(2), 16(3), 17(2), 18, 19(2), 20, 21, 22(2), 23, 24, 25(2), 26(3), 27(2), 28(2), 29(2), 30, 31, 32(3), 33(2), 34, 35, 36, 37(2), 38, 40, 41(2), 42(2), 43, 45(3), 46, 47(2), 48(2), 51, 53(2), 54(2), 57, 60, 61, 62(2), 67, 69, 87, 97(2), 100, 145, 158.

Withdrawal times: 0(6), 1(5), 2(4), 3(3), 4, 6(5), 7(5), 8, 9(2), 10, 11, 12(3), 13(3), 14(2), 15(2), 16, 17(2), 18(2), 19(3), 21, 23, 25, 27, 28, 31, 32, 34, 35, 37, 38(4), 39(2), 44(3), 46, 47, 48, 49, 50, 53(2), 55, 56, 59, 61, 62, 65, 66(2), 72(2), 74, 78, 79, 81, 89, 93, 99, 102, 104(2), 106, 109, 119(2), 125, 127, 129, 131, 133(2), 135, 136(2), 138, 141, 142, 143, 144, 148, 160, 164(3).

